

Exhibit 28

1 UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY
2
3 IN RE: VALSARTAN, LOSARTAN,)
AND IRBESARTAN PRODUCTS)
4 LIABILITY LITIGATION)
_____) MDL No. 2875
5)
THIS DOCUMENT RELATES TO ALL)
6 CASES)

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9 CONFIDENTIAL INFORMATION - SUBJECT TO PROTECTIVE ORDER
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11

VIDEO DEPOSITION OF DANIEL CATENACCI, M.D.
12 VIA VIDEOCONFERENCE
13 September 14, 2021
9:20 a.m.

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Volume 2

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18 Reporter: John Arndt, CSR, CCR, RDR, CRR
19 CSR No. 084-004605
CCR No. 1186
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<p style="text-align: right;">Page 303</p> <p>1 higher in the one -- the patients who have higher 2 comorbidity indexes, there's a higher percentage of 3 them in the exposed group. So that's an important 4 factor for sure, yes. 5 Q. And those factors can be strong 6 confounders that traditional statistical techniques 7 cannot always control; correct? 8 A. Potentially, yeah. And especially when 9 you try to -- that doesn't necessarily mean you've been 10 able to eliminate all of the confounding. 11 Q. For example, a traditional statistical 12 technique that doesn't control for those factors would 13 be the Cox model that was used here; correct? 14 A. No, I think very clearly they state here 15 that they did adjustments based on these confounding 16 variables, including all the ones we just mentioned. 17 And that said, there's still going to be potential for 18 residual confounding because these patients clearly, as 19 you've pointed out, have higher risk factors at 20 baseline for getting cancer, and so despite trying to 21 make that adjustment -- that's why all of these hazard 22 ratios are called adjusted hazard ratios -- and they go 23 through that in the methods pretty detailed -- and they 24 even adjusted by just a few of them versus all of them</p>	<p style="text-align: right;">Page 305</p> <p>1 Correct? 2 A. I missed where you said we were, but I do 3 remember it saying that, yes. 4 Q. I'm on Page 359, left-hand column, second 5 paragraph. 6 A. Okay, yeah. Uh-huh. 7 Q. Liver cancer is a specific cancer; right? 8 A. Yes, it is. 9 Q. So when you said that NDMA containing the 10 valsartan impurity was not associated with any 11 increased risk in overall cancer or with any specific 12 cancer, that's an incorrect statement; correct? 13 A. When it says any specific cancer, that is 14 inaccurate with respect to the liver finding here. 15 Q. The authors continue where I was reading. 16 "This is interesting, as from a biological perspective 17 liver cancer is the most likely form of cancer to 18 resulting from NDMA contamination." 19 That's, I guess, their viewpoint; correct? 20 A. Yes. Yes. 21 Q. Do you agree with that viewpoint? 22 A. I think that it's an interesting finding, 23 given that that is -- one of the risk factors is that 24 that's where the NDMA is metabolized, in the liver, and</p>
<p style="text-align: right;">Page 304</p> <p>1 to see if there are any major differences, and 2 ultimately there weren't any major differences. 3 But I think that we're agreeing that, 4 despite making all of those adjustments, there could 5 still be residual confounding that, as I mentioned, 6 usually would lead to a signal that's a false positive 7 signal if you don't account for an underlying factor 8 that was there. 9 Q. Let's look for a moment at your report if 10 we could. I'm looking at Page 39. And I think, for 11 the record, I just got a note from Chris that we marked 12 the Gomm study as Exhibit 14, just for the record. 13 If you could look at your report, Page 39. 14 You make a statement in the middle of the page, or a 15 little below the middle of the page. You say, "In 16 other words, taking NDMA containing the valsartan 17 impurity was not associated with any increased risk in 18 overall cancer or with any specific cancer." 19 Do you see that? 20 A. Yes. 21 Q. Looking now at Page 359 of the study, the 22 Gomm study, on the left-hand column. They state in the 23 second full paragraph, "For liver cancer, however, we 24 observed a statistically significant association."</p>	<p style="text-align: right;">Page 306</p> <p>1 that at least in the Keto (ph) studies at very high 2 doses, that's -- they do -- they have been noted to 3 have liver cancers, and that the finding here -- one of 4 many findings that's being looked at -- suggests that, 5 at least at a very, very small effect size. 6 I think that's an interesting signal that 7 comes out of this paper, that as we both mentioned has 8 confounding, could be a positive -- a false positive 9 signal based on not adjusting for a lot of different 10 things that we just talked about. 11 As we talked about earlier, it's an 12 interesting finding. Is it enough to hang your hat on 13 and call definitive, as opposed to this should be 14 assessed in an independent cohort that is looking 15 specifically at this question, as opposed to one of 16 many things? That's how I would frame the finding, but 17 it is in that context something that I would say. 18 The only other thing I would point out is 19 that in other animal models, I think I mentioned 20 earlier, is that the nonhuman primates at very high 21 doses of some of these agents don't show liver cancer 22 and that in the Gomm study, even as we both agreed that 23 there is a hypothetical potential of confounding of 24 some of the non-ZHP agents in the control arm, there</p>

<p style="text-align: right;">Page 351</p> <p>1 MR. INSOGNA: Object to form.</p> <p>2 A. There are -- I mean, there are the three</p> <p>3 ways, if I can pull up my --</p> <p>4 BY MR. SLATER:</p> <p>5 Q. Or do you not know? You can say I don't</p> <p>6 know and then I move on.</p> <p>7 MR. INSOGNA: Object to form.</p> <p>8 A. Can I -- I want to point out one area in</p> <p>9 my report just so that I state it correctly, if I can</p> <p>10 find it. The Hrudu (ph) study, which is -- okay.</p> <p>11 Right.</p> <p>12 So I was just making sure that I got the</p> <p>13 three ways in the Hrudu study that were used</p> <p>14 simultaneously to sort of look at the range that was</p> <p>15 identified, and so some of them are actually just</p> <p>16 measuring NDMA levels directly in the blood.</p> <p>17 And so if you're quantifying how much,</p> <p>18 say, for example, you're exogenously taking and you</p> <p>19 could compare how much is in the blood, you can</p> <p>20 estimate how much was endogenously created. And so</p> <p>21 your question of you can't accurately do that -- not</p> <p>22 necessarily true.</p> <p>23 You could estimate the exogenous exposure</p> <p>24 with the limitations that that has, which are far</p>	<p style="text-align: right;">Page 353</p> <p>1 than the exogenous levels in the diet.</p> <p>2 BY MR. SLATER:</p> <p>3 Q. Did you see any studies that estimated the</p> <p>4 level of endogenous formation of NDMA at not what you'd</p> <p>5 consider to be very high levels?</p> <p>6 A. There were a range, I think, as we talked</p> <p>7 about, at various extremes, but even at the lowest</p> <p>8 levels they were higher -- much higher than, say, the</p> <p>9 FDA ADI, as an example.</p> <p>10 Q. Well, for example, did you see any studies</p> <p>11 that estimated the level at perhaps 1,000 nanograms a</p> <p>12 day?</p> <p>13 A. I believe that 1,000 nanograms a day,</p> <p>14 which is about 100 times the 96 nanograms that the FDA</p> <p>15 has indicated as an acceptable level, so that's my</p> <p>16 point, is that there are orders of magnitude even at</p> <p>17 the lowest estimates. That's all I'm saying.</p> <p>18 So I think in the end I'd agree with you</p> <p>19 that I'm not here to opine on what's the appropriate</p> <p>20 way to do it, but I'm looking at all of the body of</p> <p>21 literature that's talking about endogenous formation,</p> <p>22 how to calculate it, and the range -- the lower level</p> <p>23 of the range is far higher, let alone probably the more</p> <p>24 likely is about -- the actual true way of doing it is</p>
<p style="text-align: right;">Page 352</p> <p>1 lower, and then evaluate how much is in the blood and</p> <p>2 deduce that there's endogenous creation, because it's</p> <p>3 much higher in the blood than what you've estimated</p> <p>4 that was being taken externally.</p> <p>5 BY MR. SLATER:</p> <p>6 Q. You're saying that's one potential</p> <p>7 approach, but you're not giving an opinion to a</p> <p>8 reasonable degree of scientific certainty that that's</p> <p>9 the accurate approach; right?</p> <p>10 MR. INSOGNA: Object to form.</p> <p>11 A. You asked me if it's possible and what's</p> <p>12 the rationale of it, and it's been done and shows that,</p> <p>13 yes.</p> <p>14 BY MR. SLATER:</p> <p>15 Q. But you agree with me you're not reaching</p> <p>16 an opinion that, for example, the Hrudu model is the</p> <p>17 right one and the other models are wrong? You're just</p> <p>18 saying this is one person who came up with this way to</p> <p>19 do it and you're pointing it out?</p> <p>20 Do I understand correctly?</p> <p>21 MR. INSOGNA: Object to form.</p> <p>22 A. There are multiple ways to do it and I</p> <p>23 tried to show that there are various ways to do it and</p> <p>24 that overall the answer is always that it's much higher</p>	<p style="text-align: right;">Page 354</p> <p>1 above that.</p> <p>2 Q. Are you saying that 1,000 nanograms a day</p> <p>3 of intake of NDMA would be a very high level?</p> <p>4 A. No, I'm saying it's a lot higher than 96</p> <p>5 nanograms, which was the FDA's accepted daily intake.</p> <p>6 And this is on routine daily living. That's -- I think</p> <p>7 that's the point.</p> <p>8 Q. Just to come back to my question --</p> <p>9 because I got to know how far we have to go and if I</p> <p>10 have to go start picking up articles in the other</p> <p>11 room -- you're not offering an opinion that there's a</p> <p>12 certain level of endogenous formation -- you're saying</p> <p>13 this is the level that I'm assuming is formed?</p> <p>14 You're just telling me there are studies</p> <p>15 that have measured it with various methods at various</p> <p>16 levels; correct?</p> <p>17 MR. INSOGNA: Object to form.</p> <p>18 A. Yes, other than what we've already</p> <p>19 mentioned in my previous responses.</p> <p>20 BY MR. SLATER:</p> <p>21 Q. I need to understand this. I didn't see</p> <p>22 an opinion in your report where you quantified an</p> <p>23 assumption as to the level of endogenous formation of</p> <p>24 NDMA in the human body.</p>

<p style="text-align: right;">Page 355</p> <p>1 You're not offering a specific opinion as 2 to a specific level; right? 3 MR. INSOGNA: Object to form. 4 A. No, other than the ranges that I put in my 5 report. 6 BY MR. SLATER: 7 Q. And when you refer to the ranges in your 8 report, you're pointing out that there are different 9 models and different ranges have been presented and 10 that's as far as you're going in terms of quantifying 11 endogenous formation; right? 12 A. Yes. 13 Q. And you also hold out the -- for the -- 14 rephrase. 15 You also agree with me that these models 16 may all be wrong and it may turn out the levels are 17 much lower; right? 18 MR. INSOGNA: Object to form. 19 A. There's no evidence about that. We're 20 always happy to evaluate new data. That's how science 21 works. But currently the data suggests that this is 22 the way to do it, that the levels are extremely high. 23 BY MR. SLATER: 24 Q. You don't have an opinion as to what the</p>	<p style="text-align: right;">Page 357</p> <p>1 right? 2 MR. INSOGNA: Object to form. 3 A. That's not what I'm using endogenous 4 amounts for. 5 BY MR. SLATER: 6 Q. I'm not asking about endogenous. I'm 7 asking you -- 8 A. I'm telling you -- you're asking if 1,000 9 nanograms per microgram -- if 1,000 nanograms per day 10 is a high level? 11 Q. In a pill of valsartan. 12 MR. INSOGNA: I'm sorry. I missed the 13 question. 14 BY MR. SLATER: 15 Q. I'll ask it again. Let me -- we'll start 16 over. 17 Do you agree that 1,000 nanograms of NDMA 18 in a valsartan pill would be a high exposure? 19 MR. INSOGNA: I just want to make sure I'm 20 clear. You're saying 1,000 nanograms, is your 21 question? 22 MR. SLATER: Yes. 23 A. A high exposure relative to what? 24 Relative to the FDA level that's high --</p>
<p style="text-align: right;">Page 356</p> <p>1 level of endogenously-formed NDMA is in the human body? 2 You don't have an opinion as to a specific 3 level, do you? 4 MR. INSOGNA: Object to form. Vague. 5 A. Not other than what I've put in my report 6 that there's a range that's very high compared to the 7 question at hand here and the questions at hand, no. 8 BY MR. SLATER: 9 Q. Your opinion is that there's a potential 10 range and that potential range may have some high 11 figures in it, but you're not saying, "In my opinion, 12 this is the right number," because you haven't 13 evaluated that issue or calculated it; right? 14 A. I'm not saying that it's one number. I'm 15 not saying it's a potential range. It is a clear range 16 that's been reported in the literature of a high -- 17 very high amount and then the low end is still high 18 compared to the levels we're talking about at the FDA 19 level. There is a clear range -- not a potential 20 range. It's a range that we see in the literature. 21 Q. If a valsartan pill had 1,000 nanograms of 22 NDMA in it -- let me start over. 23 If a valsartan pill had 1,000 nanograms of 24 NDMA in it, you would agree that's a high exposure;</p>	<p style="text-align: right;">Page 358</p> <p>1 BY MR. SLATER: 2 Q. You just said 1,000 nanograms would even 3 be a high level of NDMA. I'm asking, does that hold 4 true when it's in a pill sold by the people that hired 5 you? 6 Is it still a high level if it's in the 7 pill from the people that hired you? 8 MR. INSOGNA: Object to form. 9 Misstates -- 10 BY MR. SLATER: 11 Q. Or does it now become a low level because 12 they're responsible for it? 13 MR. INSOGNA: Object to form. Misstates 14 his testimony. 15 A. I'm trying to tell you that through 16 routine living we have high levels -- 1,000 nanograms 17 is at the lowest estimate of that -- just from living 18 and eating, and that these levels are extremely higher 19 than what the FDA has shown, has reported, or has put 20 out as a threshold of what's safe. That's all I'm 21 saying. 22 And so what you're asking now, is an extra 23 1,000 nanograms a lot? No, not in the context of that 24 sea of exposure that we're exposed to all the time just</p>